Stroke Volume During Orthostatic Challenge: Comparison of Two Non-Invasive Methods

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Background: Real time non-invasive determination of stroke volume (SV) is important to astronaut orthostatic testing. We compared simultaneous estimates of SV calculated from peripheral pulse waveforms with a more conventional non-invasive technique. ***Methods:*** Ten men and nine women completed 12-min protocols. The relative change (%Δ) in beat-to-beat SV was estimated non-invasively from changes in pulse waveforms measured by application of infrared finger photoplethysmography (IFP) and thoracic impedance cardiography (TIC). The %ΔSV values were calculated from continuous measurements in the supine posture and over the first 10 s (T1), second 10 s (T2), and 3 min (T3) of 80° head-up tilt (HUT). ***Results:*** Average %ΔSV measured by IFP at T1 (−11.7 ± 3.7%) was statistically less than the average %ΔSV measured by TIC at T1 (−21.7 ± 3.1%), while average %ΔSV measured by IFP at T2 (−16.2 ± 3.9%) and T3 (−19.1 ± 3.8%) were not statistically distinguishable from the average %ΔSV measured by TIC at T2 (−21.8 ± 2.5%), and T3 (−22.6 ± 2.9%). Correlation coefficients (r^2) between IFP and TIC were 0.117 (T1), 0.387 (T2), and 0.718 (T3). ***Conclusion:*** IFP provides beat-to-beat (real-time) assessment of %ΔSV after 20 s of transition to an orthostatic challenge that is comparable to TIC. IFP technology flown during space missions can be used to assess physiological status and countermeasure effectiveness for orthostatic problems that may arise in astronauts after spaceflight. While the peripherally measured IFP response is delayed, the ease of implementing this monitor in the field is advantageous.

Keywords: photoplethysmography, impedance cardiography, tilt table testing.

ORTHOSTATIC HYPOTENSION and syncope have proven to be debilitating for astronauts returning from space, leading to presyncope and intolerance in approximately 40% of crewmembers (1,6,11,17). As a result, real-time assessments of cardiovascular function and hemodynamic responses during passive stand and tilt tests can be critical to the flight surgeon's ability to provide early detection of imminent orthostatic instability and apply appropriate therapeutic action. Traditional vital sign monitoring of BP and pulse rate using standard sphygmomanometry has been used in post-spaceflight clinical cardiovascular assessments and orthostatic tests (1,9–13,17). However, development of orthostatic hypotension and impending intolerance (presyncope) can occur too rapidly for traditional sphygmomanometric techniques to assist the flight surgeon in early diagnosis and application of effective intervention. On the other hand, low stroke volumes or peripheral vasoconstriction have some predictive value in orthostatic testing (1–3,10,11,17). Therefore, the ability to obtain continuous noninvasive measures of change in stroke volume could prove valuable to flight surgeons in their clinical assessment and treatment of astronauts following spaceflight.

Stroke volume has been measured during orthostatic testing using echocardiography or thoracic impedance cardiography (TIC). The clinical usefulness of both techniques can be limited by body movement and inability to calculate and display stroke volume real-time data. The emergence of infrared finger photoplethysmographic (IFP) technology has been introduced as a method of providing continuous non-invasive estimation of stroke volume simultaneously with arterial BP (7,18). The ability to obtain continuous beat-to-beat stroke volume and BP independent of changing body posture is an attractive feature because it provides the capability of obtaining real-time estimates of total peripheral vascular resistance. However, we are unaware of any investigation designed to provide a systematic comparison of the continuous measurement in stroke volume by IFP with some other acceptable non-invasive technique. The purpose of this investigation was, therefore, to compare stroke volume responses estimated by IFP during a standard tilt test protocol with measurements of stroke volume obtained from TIC.

METHODS

Subjects: There were 19 healthy, non-smoking subjects (10 men and 9 women) who volunteered to participate in the present investigation. The subjects were normotensive with systolic BP = 127 ± 3 mmHg and

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diastolic BP = 68 ± 2 mmHg. Their average (±SE) age, height and weight were 34 ± 3 yr, 172 ± 2 cm, and 70.1 ± 3.9 kg. The subjects were not astronauts, neither trained specifically for this study, nor taking prescription medication to control hemodynamic function. A complete medical history and physical examination that included a resting 12-lead ECG and clinical orthostatic exam (supine/seated/standing consecutive BP measurements) were obtained on each of the potential subjects. During an orientation period that preceded each experiment, all subjects were made familiar with the laboratory, the protocol, and procedures. Experimental procedures and protocols were reviewed and approved by the Institutional Review Board of the Kennedy Space Center for the use of human subjects. Each subject gave written informed voluntary consent to participate in the experiments.

Protocol: Each subject completed a head-up tilt table test (HUT) during spontaneous breathing through a face mask with an impedance threshold device (ITD; Advanced Circulatory Systems Inc., Eden Prairie, Minnesota) set at an inspiratory resistance of approximately −7 cm H_2O resistance. A detailed description of the ITD and its functional application during an orthostatic challenge has been reported elsewhere (4). Subjects maintained a supine posture for 30 min prior to the start of data collection. At the start of data collection (indicated as time (T) = 0:00), recordings for SV determination were initiated as subjects breathed through a plastic medical facemask. At T = 3:45 min, the ITD valve was attached to the facemask and the subject was instructed to breath on the ITD with natural but deep breaths. At T = 4:00 min, subjects were tilted to 80° head-up tilt (HUT) and maintained this position for 4 min. At T = 8:00 min, subjects were returned to the supine position. Measurements of stroke volume were collected continuously throughout the baseline and HUT periods, and stored on a data acquisition system based in LabView®. Relative (percent) changes in stroke volume were determined from the 10-s average of beat-to-beat analysis during three time periods: 1) the initial 10-s period starting immediately on the assumption of HUT (T1); 2) the second 10-s period (10 to 20 s) after the assumption of HUT (T2); and 3) at 3 min after the assumption of HUT (T3). Measurements during T1 and T2 reflected the transition from supine baseline to upright posture while measurements at T3 were chosen to obtain a comparison during a steady-state condition. Each experimental session was conducted over a period of less than 90 min.

Stroke volume measurements: Beat-to-beat stroke volume (SV) was estimated non-invasively from changes in pulse waveforms measured by application of IFP with the Portapres® (Finapres Medical Systems, Amsterdam, The Netherlands). Stroke volume estimation by application of IFP is based on computed aortic flow pulsations from arterial pressure waveforms by simulating a nonlinear, time-varying three-element model (aortic characteristic impedance, arterial compliance, and systemic vascular resistance) of aortic input impedance (18). Two of the model parameters, characteristic impedance and arterial compliance, are derived from an aortic pressure-area relationship applying the arctangent model of aortic mechanics. The third element, total peripheral resistance, is not known, but is an outcome of the model simulation.

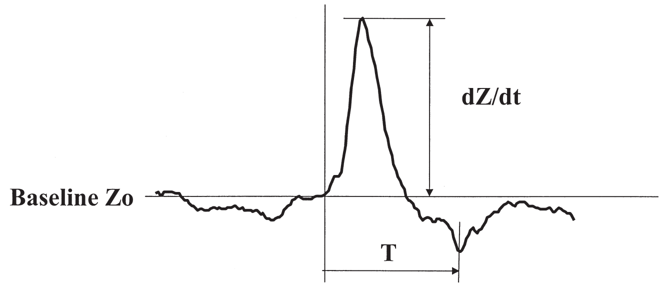

Fig. 1. Example of an analog signal tracing of the electrical impedance cardiogram waveform used to determine baseline thoracic impedance (Z_0), the change in impedance over time (dZ/dt), and the ventricular ejection time (T).

Thoracic impedance (Z_0) was measured using four circumferential electrodes, two placed around the base of the neck and two placed around the thorax just below the xiphoid process. A bioelectric impedance cardiograph unit (HIC-2000, Bio-impedance Technology, Inc., Chapel Hill, NC) was used to introduce a constant current of 4 mA at 100 KHz frequency across the outer electrodes and detect changes in electrical impedance with each pulse beat across the inner pairs of electrodes (8). The analog signal of the electrocardiogram waveform (ECG), baseline (Z_0), and the change in impedance over time (dZ/dt) were converted to a digital signal for analysis using National Instruments LabView software (**Fig. 1**). The following algorithm was used to estimate SV from the ECG and impedance (8):

$$SV = \frac{\rho L^2 T (dZ/dt)_{min}}{Z_0^2}$$

Where:

ρ = the average electrical resistivity of blood at 100 KHz (150 ohm-cm);

L = the mean distance between the two inner electrodes in cm;

T = the ventricular ejection time in seconds as measured from the dZ/dt and ECG waveforms.

The relative change in SV (%ΔSV) from supine to HUT was calculated as follows:

$$\%\Delta SV = [(\text{pre-tilt SV} - \text{post-tilt SV})/\text{pre-tilt SV}] * 100$$

Statistical analysis: We performed a standard two-method (IFP, TIC) *t*-test statistical analysis to determine differences in relative (percent) SV change from supine to upright posture between the two techniques for SV measurement for each separate period of assessment (i.e., T1, T2, T3). Exact p-values were calculated for each independent effect and reflect the probability of obtaining the observed or greater effect given only random departure from the assumption of no effects. Standard errors are raw measures of variation about the specific treatment group mean. Standard Pearson product correlation coefficients were performed to quantify the relationship between the two techniques for SV measurement at each of the three time periods of assessment.

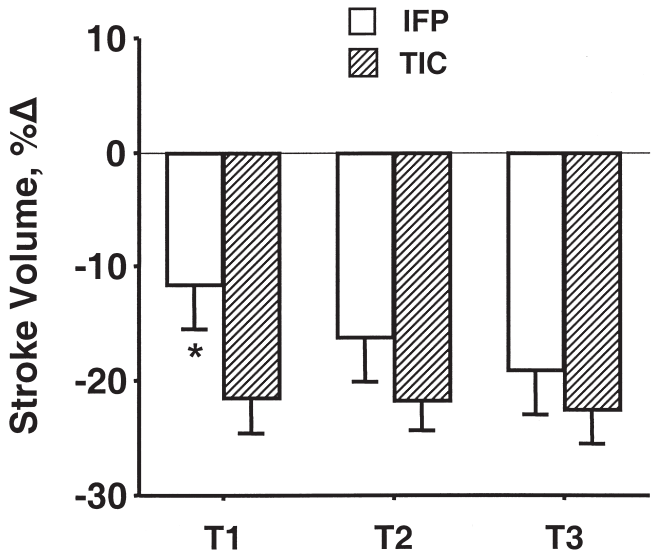

Fig. 2. Mean ± 1 SE values for 19 subjects of percent change (%Δ) in stroke volume comparing infrared finger photoplethysmography (IFP; open bars) with thoracic impedance cardiography (TIC; lined bars) recorded during T1, T2, and T3 of 80° head-up tilt. *Difference (p < 0.02) compared with TIC.

RESULTS

The average %ΔSV measured by IFP during HUT at all time intervals was less than that measured by TIC (**Fig. 2**). The average %ΔSV measured by IFP at T1 (−11.7 ± 3.7%) was less (p < 0.02) than the average %ΔSV measured by TIC at T1 (−21.7 ± 3.1%), while the average %ΔSV measured by IPF at T2 (−16.2 ± 3.9%) and T3 (−19.1 ± 3.8%) were not statistically distinguishable (t ≤ 1.019; p ≥ 0.322) from the average %ΔSV measured by TIC at T2 (−21.8 ± 2.5%), and T3 (−22.6 ± 2.9%). The relationships between individual values of %ΔSV comparing IFP with TIC at T1, T2, and T3 of 80° head-up tilt are presented in **Fig. 3**. For T1, the linear equation is %ΔSV [IFP] = 0.53%ΔSV [TIC] – 0.2 (r^2 = 0.177); for T2, the linear equation is %ΔSV [IFP] = 0.94%ΔSV [TIC] – 2.5 (r^2 = 0.387); and for T3, the linear equation is %ΔSV [IFP] = 0.78%ΔSV [TIC] – 7.0 (r^2 = 0.718).

DISCUSSION

IFP, in addition to standard sphygmomanometry, has been used to monitor BP in astronauts during their clinical orthostatic tests immediately after spaceflight (1,11,17). Unfortunately, conventional BP measurement techniques have not proven to be a reliable or early indicator of the onset of syncope, since some astronauts who became orthostatically intolerant and could not finish a 10-min stand test after return from a space mission demonstrated no change in BP while others showed gradual or abrupt reductions just prior to their presyncopal event (1). However, low stroke volume and a limited ability to increase peripheral resistance have been associated with orthostatic intolerance after spaceflight (1–3,11,17). It, therefore, seems that a non-invasive continuous assessment of central (stroke volume) and peripheral (vascular resistance) hemodynamics would prove a more sensitive clinical tool in

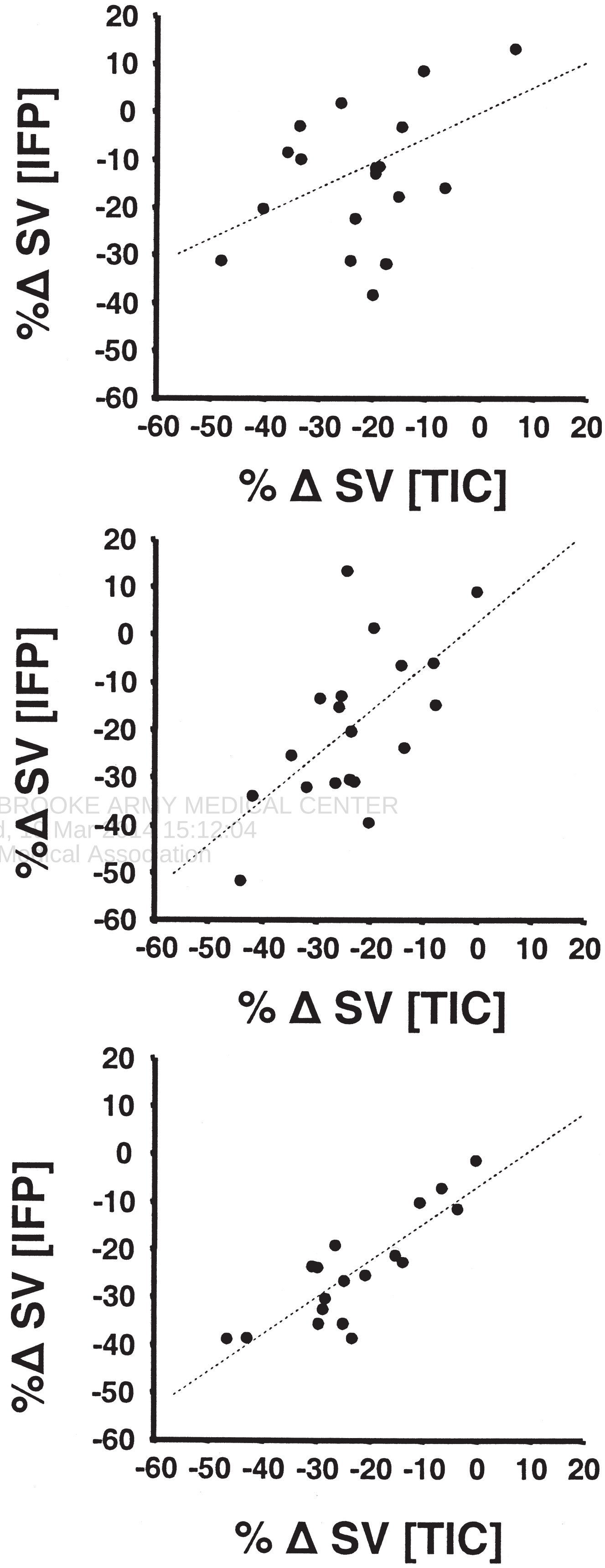

Fig. 3. Individual values for 19 subjects of percent change (%Δ) in stroke volume (SV) comparing infrared finger photoplethysmography (IFP) with thoracic impedance cardiography (TIC) recorded during T1 (top), T2 (middle), and T3 (bottom) of 80° head-up tilt.

predicting the orthostatic compromise to astronauts during and after re-entry than BP alone. Although TIC has provided an effective noninvasive technique for the measurement of SV in human subjects (14), the requirement for electrodes and sensitivity to body and respiratory movements can make its use difficult in the operational environment. In contrast, IFP requires only the placement of a small pneumatic cuff around the middle finger. With this perspective, we compared the relative change in beat-to-beat stroke volume obtained from the same IFP methodology used to measure BP with changes in SV measured continuously with noninvasive TIC. Our results demonstrated that, given a transient time delay of at least 20 s to reach a hemodynamic steady-state, IFP provided a non-invasive beat-to-beat measurement of percent reductions in stroke volume during a standard clinical tilt table protocol similar to that used to test astronauts.

Both IFP and TIC tracked reductions in stroke volume during the transient and steady-state phases of moving from the supine to head-up position. However, IFP significantly underestimated the %ΔSV measured by TIC and accounted for only about 18% of the total variance of the %ΔSV measured by TIC during the initial phase (T1 = 10 s) of transition from supine to HUT. On the other hand, the measure of %ΔSV and intra-subject variability improved substantially with measurements conducted later in time from the transient phase (i.e., steady-state). This distinct difference between mean values and correlation coefficients generated from %ΔSV measurements with IFP and TIC during transient and steady-state phases of posture change provides unique insight into the limitation of using peripheral vascular responses to assess SV changes. The reduction in stroke volume during orthostatic challenges is closely related to a proportional (linear) elevation in sympathetic nerve activity (3,10). Increased sympathetic nerve activity in turn causes reductions in arterial pulse wave magnitude through vasoconstriction. Since sympathetic activity controls peripheral vascular resistance, it is not surprising that changes in peripheral arterial waveforms would track changes in stroke volume. During the initial seconds of transition in posture from supine to HUT, a rapid mechanical redistribution of blood from the central circulation toward the lower extremities (blood pooling) causes an immediate reduction in cardiac filling and stroke volume (15). The subsequent reflex-mediated increase in sympathetic nerve activity is manifested in reductions in the magnitude of peripheral arterial pulse waveforms only after a time delay of ~10 s (5,16). This mismatch between the immediate change in central hemodynamics (i.e., reduction in cardiac filling and stroke volume) and a delay in sympathetically mediated reflex vasoconstriction was manifested in the present investigation by the large difference and variability between IFP and TIC measurements obtained during the transition phase from supine to HUT postures. As sympathetically mediated vasoconstriction approached complete compensation following the transient phase of the HUT maneuver, there was little difference between average %ΔSV measured by IFP and TIC with about 72% of the total variance in the %ΔSV accounted for. It is clear from our results that more realistic values of %ΔSV will be obtained with IFP when measurements are conducted after the transient phase of blood volume redistribution.

Limitations

Both IFP and TIC are non-invasive techniques for estimating stroke volume that were not compared with a standard invasive technique. Therefore, we cannot dismiss the possibility that either or both IFP and TIC provided inaccurate measurements of absolute SV values. However, there is compelling evidence in the published literature providing comparisons and significant agreements of both IFP and TIC. Estimates of stroke volume using TIC have been reported with correlation coefficients of 0.70 to 0.93 in comparison with thermodilution techniques (14). Likewise, comparisons of 76 cardiac output measures using IFP during open-heart, bypass surgery in 8 patients produced a mean deviation of ± 2% (with SD of 8%) when compared with 76 simultaneous thermodilution measurements (18). Further, we chose to analyze our SV data as percent changes from baseline since TIC and IFP comparisons with thermodilution are improved when presented as relative changes (14,18).

Operational Implications

Like TIC, IFP provides a simple non-invasive, beat-to-beat measure of SV. However, IFP offers several advantages over TIC. Technically, the absence of requirement for electrodes makes IFP application faster and easier for the attending health provider. In addition to central hemodynamic measurements (i.e., HR, SV and cardiac output), IFP provides concurrent measures of beat-to-beat arterial BP. Thus, with cardiac output and BP measurements, IFP offers the capability to calculate total peripheral vascular resistance, which has proven to be a predictor of orthostatic tolerance. It should be emphasized that more realistic values of %ΔSV will be obtained with IFP when measurements are conducted after the transient phase of blood volume redistribution.

There are three other considerations to be understood during field implementation of the IFP technique. The current version of the Portapres® automatically compensates for the hydraulic difference between the vertical locations of the finger cuff and the heart. In this protocol, the finger was kept at heart level throughout the HUT by attaching the arm to an outstretched armboard to assure accuracy. Earlier use of this instrumentation utilized an open finger golf glove attached by Velcro® to the clothing over the heart. A second consideration is the assurance of good circulation in the fingers. Our experience during rescue operations with hypothermic subjects included poor measurements associated with reduced blood flow in the hands (D. Doerr, unpublished observations). Consequently, maintenance of body (hand) warmth may be required to obtain valid measurements. The third concern is accurate placement of a properly sized cuff on the finger.

Experience is quickly gained in locating the cuff by comparison with conventional occlusive BP techniques.

With these simple factors in mind, measurements from peripheral arterial pulse waves are easily implemented and independent of body and respiratory motion, which makes IFP more readily applicable for monitoring astronauts and other crewmembers in the austere aerospace environment.

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